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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,390	01/22/2004	Koral Embil	511-1001	2411

51523 7590 04/13/2010

LOUIS C. PAUL
420 East 61st Street, 8E
NEW YORK, NY 10021

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
04/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,390	EMBIL ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-14,16-26 and 31-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14,16-26 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendments and responses dated 9-26-09 & 12-18-09 is acknowledged.

Claims 1, 2, 15, and 27-30 have been canceled. New claim 36 has been added by amendment of 12-18-09.

Claims 3-14, 16-26 and 31-36 are pending.

In light of the amendment, the following is a new rejection:

Claim Objections

1. Claim 31 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Instant is dependent upon claim 3, which is indirectly dependent upon claim 36. While instant claim 36 limits the viscosity of each of the emulsions to be between 5000 to 15000 cps, instant claim recites a viscosity (less than 20000, which is above the range of 15000 cps) that is outside the range claimed in claim 36 and thus fails to further limit the previous claim.

Claim Rejections - 35 USC § 112

2. Claims 3-14, 16-26 and 31-36 are rejected less than 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant claim 36 recites the new limitation, "wherein the polymeric delivery system comprises about 5% to about

60% by weight of active ingredient, with the proviso that the active ingredient is not a retinoid, and comprises about 1% to about 20% when the active ingredient is a retinoid", which is not supported by the instant specification.

3. Applicants state in their response dated 12-18-09 that literal support in the specification for the amendment is found in the text expressly incorporated supra. However, a review of the instant specification does not provide any support for the claimed percentages of active agents or retinoid in the delivery system. The description on pages 14, 19-20 or 24 does not support the claimed percentages.

The following rejection of record has been maintained:

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 3-14, 16-26 and 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/912726 (WO) in view of US 7,060,732 to Vishnupad et al ('732) and US 5,955,109 to Won et al ('109) **or alternatively,** over WO in view of '732, '109 and EP 306236 (hereafter EP).

6. Instant independent claim 36 recites A pharmaceutical and/or cosmetic product comprising first and second emulsion formulations for topical administration to the skin, hair or nails of a mammal, wherein: each emulsion formulation has a viscosity of 5,000 cps to 15,000 cps, and comprises: (i) a water-based carrier base, the water-based

carrier bases of the first and second emulsion formulations having substantially the same lipophilicity, (ii) a non-aqueous phase, and (iii) at least one active ingredient, wherein the active ingredient in the first and second emulsions are different; at least one of the emulsion formulations includes a non-swellable and cross-linked polymeric delivery system comprised of polymers capable of entrapping and controlling the release of at least one active ingredient, wherein the polymeric delivery system comprises about 5% to about 60% by weight of active ingredient, with the proviso that the active ingredient is not a retinoid, and comprises about 1% to about 20% when the active ingredient is a retinoid; the pharmaceutical and/or cosmetic product further comprising storage means whereby said formulations are maintained separately prior to dispense, together with dispense means which permit said formulations to be dispensed from said storage means.

7. WO teaches a package comprising components which, upon being mixed, are capable of forming a pharmaceutical composition that is effective in treating acne, one of the components comprising an oxidizing agent and another of the components comprising an antibiotic which is effective against acne-associated bacterial species, the components separated one from the other in the package, one component having a viscosity within about 50 % of the viscosity of the other component. WO teaches that the package components which, upon being mixed, are capable of forming a pharmaceutical composition that is effective in treating ache, one of the components comprising a benzoyl peroxide gel and another of the components comprising a gel of

erythromycin and hydroxypropylcellulose; and containers for holding the components in the package separated one from the other; the components having viscosities such that, upon the application of a uniform forces to the components, substantially equal volumes of the components are capable of being dispensed simultaneously from the containers (abstract, page 7, L 1-10-12 and l 23-27).

8. WO teaches combination of clindamycin or erythromycin with benzoyl peroxide and thus meets the instant claims 36, 3-8, 11-14.

9. WO teaches a hydroxylated vinylic polymer as a gelling agent but not state if the polymer is capable of entrapping as in the instant claim 36, or if the polymer is crosslinked and non-swollen.

10. For the description of the packaging means, see pages 8-9 of WO reference and meets instant claims 5 and 6.

11. WO states that the composition is stable on storage (page 11).

12. For the claimed viscosities (5,000 cps-15,000 cps) and the forms of the components, WO states that the viscosities may be same or different and when combined the components should yield the desired viscosity and that the components may range from solids to liquids such as gels, creams, lotions etc (page 23, L 1-12, l 21-page 24, L 7), allowing the user to dispense amounts that are substantially equal. WO teaches viscosities in the range of 200000 (page 25) and not the claimed 5,000 cps-15,000 cps. In addition to the antibiotic clindamycin, WO teaches several actives such as tretinoin, antifungal compounds etc (page 27).

13. For the claimed phases, WO does not teach emulsions, but teaches that the active agents are dissolved in water or other solvents depending on their solubility (page 28) and further teaches addition of surfactants for even distribution of compounds such as benzoyl peroxide (page 30).

14. WO does not teach the claimed entrapping polymers. WO also lacks the teaching of substantially same lipophilicity of the carrier bases in the two emulsions.

15. Applicants admit in the instant specification that 109 teaches the claimed entrapping porous polymers (microsponge) that comprises the same monomeric units as that of instant claim 3 (see abstract). The composition of '109 is effective for treating acne. It is stated that retinoic acid is trapped inside and diffused in controlled manner from the microsponge (col. 2), based on the pore volume (col. 3, L 14-24). The porous polymeric beads or microspheres of '109 have the same pore diameter, particle size shape as claimed in the instant claim 3 (col. 4, L 150) and are made of the same components as instant (col. 6-7). In addition to retinoic acid, '109 also teach compositions containing porous polymers that entrap benzoyl peroxide (see example in col. 8) as an active ingredient.

16. '109 expressly states that the activity-time curve of the vitamin is extended and flattened out. The magnitude of the release arte is controlled by the pore volume distribution in the microsphere itself, notably the pore volume and the average pore diameter (col. 3, L 14-23) and that the active agent is diffused in to the solvents or bodily fluids (col.2, L 65-68). '109 further states that once dried microspheres with active agent impregnated are prepared, they are further applied to the skin in appropriate

compositions such as gels, lotions etc., and employing suitable liquid vehicles. '109 teaches that when liquid vehicles are used and the impregnant is a solution of an active agent in a solvent, the solvent and the vehicle must be immiscible so that the outward diffusion of the active agent will not be accelerated by mutual diffusion between the solvent and the vehicle. '109 suggest employing appropriate combinations of polar vehicle and a nonpolar vehicle, a polar and a nonpolar solvent.

EP also teaches controlled release of several skin care and hair care active agents such as benzoyl peroxide, salicylic acid, minoxidil etc., from a composition containing a microsponge polymeric system (the same microsponge as that claimed in the instant invention). In particular, EP (as well as Wester) teaches the treatment of acne with benzoyl peroxide. For the various active agents of EP, see pages 2-5, 7, page 12, L 40-45 and examples and on page EP teaches a number of combinations of the active agents.

17. Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ the microsponge polymeric delivery material of '109 in the composition of WO, either in one or both compartments, because EP as well as 109 suggests that the porous polymeric material forms a continuous network open to the exterior particles, permitting outward diffusion of the impregnated active agents in a controlled fashion. '109 further suggests that the entrapment of the active agent in the porous network of the polymer enables withstanding of higher concentrations of active agent without causing side effects such as irritation, and also the pores are interconnected and open to the particle surface to an extent that

substantially full communication is provided between the internal pore space and the exterior of the particle.

18. For the amounts of the active agents in the instant claims, both WO and '109 references teach the amounts that meet the claim limitations.

19. Neither WO nor '109 teach the emulsions formulation of first and second ingredients and of substantially same lipophilicity of the carrier bases in the two emulsions. However, both are directed to acne treating compositions.

'732 also teach acne treating compositions comprising separately packaged active ingredients with a common dispenser (abstract and col. 2, L 40-57). In particular, '732 teach benzoyl peroxide and antibiotic or antibiotic and retinoid combinations (col. 2, l 58-64. While '732 states the compositions are substantially anhydrous, they state that if the composition is not water sensitive it is still allowed so as to prepare emulsions(col. 3, L 60-65 & col. 6). '732 state that the composition may have a viscosity in the range of 10,000 to 1,000,000 cps (col. 6, L 19-24 and l 45-47). '732 further teaches preparation of benzoyl peroxide compositions where the compositions contain surfactant and according to '732 the first and second compositions may be in the form of a gel, emulsion, lotion etc (col. 3, L 25-35).

All of the references cited teach two compartment dispenser containing first and second actives for acne treatment, in particular, the same actives i.e., benzoyl peroxide, antibiotic, retinoic acid etc. All of the references also desire viscosities of the compositions such that the compositions may be easily pumped. Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant

invention to prepare an appropriate emulsion formulation of the first and second compositions of WO depending on the solubilities of the active agent (suggested by WO or '732) and further optimize the viscosities of the two compositions in the package so as to be able to dispense the desired amounts of the two components either equal or varying amounts because '732 suggests viscosities greater than 5000, ranging from 10000 to 100000 for presenting good feel to the user and also that the viscosities differ by no greater than25% between the first and second compositions and WO suggests that the viscosities may vary as long it enables the user to dispense the desired (same or varying) amounts from two compartments. Applicants have not provided any unexpected advantage of the claimed viscosity and further '732 suggests lower viscosity ranges.

With respect to lipophilicity, applicants failed to establish any unexpected advantage of the substantially same lipophilicity whereas the references suggests the same compositions i.e., emulsions in both compartments. Further, the teachings of '109 suggests to one skilled in the art when liquid vehicles are used and the impregnant is a solution of an active agent in a solvent, the solvent and the vehicle must be immiscible so that the outward diffusion of the active agent will not be accelerated by mutual diffusion between the solvent and the vehicle. '109 suggest employing appropriate combinations of polar vehicle and a nonpolar vehicle, a polar and a nonpolar solvent. Further, 109 patent states that magnitude of the release arte is controlled by the pore volume distribution in the microsphere itself, notably the pore volume and the average pore diameter (col. 3, L 14-23) and that the active agent is diffused in to the solvents or

bodily fluids (col.2, L 65-68). Therefore, it would have been obvious for a skilled artisan at the time of the instant invention was made to choose the variables such as optimum pore size, pore volume of the polymer entrapping active agent and also adjust the polarity of the solvent used in the delivery vehicle depending the solubility of the active agent entrapped inside the porous network of polymers and the desired release rate of the active agent. In this regard, applicants have not provided any unexpected advantage of two carrier bases having substantially same lipophilicity.

Response to Arguments

20. Applicant's arguments filed 9-26-09 and 12-18-09 have been fully considered but they are not persuasive.

21. Applicants argue that the description of the component compositions in WO '726 is limited in that the final composition is taught to be of sufficient viscosity to adhere to the skin for sufficient time to be therapeutically effective. It is argued that WO '726 does not, however, teach or suggest that the active ingredients are contained (i.e., entrapped) within a polymeric delivery system (as that term is use in Applicants' claims). It is argued that Vishnupad neither teaches nor suggests use of a polymeric delivery system (as that term is used in Applicants' claims) and

22. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.

1986). The rejection includes the teachings of '109 patent and EP for the claimed polymers.

23. It is argued that Vishnupad likewise discloses a "dual [chambered] dispenser" in which components of an acne-treating composition are separately stored. Vishnupad discloses that it is strongly preferred that one of the components ("compositions") is substantially anhydrous. Compositions claimed in Vishnupad are not substantially anhydrous. With respect to Won ('109 patent), it is argued that Won discloses controlled-release compositions for topical delivery of retinoic acid. More particularly, the retinoic acid is retained within the pores of porous solid particles or microspheres. These porous polymeric microbead carriers (retaining the retinoic acid) may be used alone or incorporated as dispersion in a "suitable vehicle". See Won, Col. 2, lines 41 - 45.

24. Applicants arguments are not persuasive because Vishnupad teaches that first or second components may be in the form of emulsions or may be anhydrous (col. 2, L 48-50 & col. 6, L 54-60). Vishnupad also teaches that depending on the stability of the active, it can be either anhydrous or aqueous; and that if the actives are not water sensitive, they can be in the form of aqueous formulations, including emulsions (col. 6, L 54-63). Thus, Vishnupad not only teaches anhydrous but also emulsion compositions.

25. It is argued that equally, if not more importantly, WO '726, Vishnupad, EP and Won are silent concerning any requirement for the lipophilicity of the components. Applicants state that according to the instant specification, carrier bases with substantially same lipophilicity is an important feature which may facilitate particularly

ready, uniform and is thermodynamically favorable mixing of the formulations. More importantly, it ensures consistent release of active ingredient from the polymeric delivery system or systems. The release properties of such systems are dependent on the physical properties of the carrier in which they are dispersed, including pH and viscosity; thus, the degree of lipophilicity is particularly important since it affects the partition coefficient of active ingredient between the polymer particles of the delivery system and the carrier and thus controls the rate of release of active ingredient from the particles into the carrier and thus to the skin. By using carriers with substantially identical lipophilicity, the products may be designed to ensure that a desired rate of release from the polymeric delivery system is consistently achieved after the formulations have been mixed and applied to the skin. Applicants further state that controlling the rate of release of the active ingredients (and, therefore their partition coefficients into the vehicle) is the key to this invention since it provides both for extended efficacy as well as reduces the potential irritancy of the final product.

26. While it is true that none of the cited references recite the claims phrase "substantially same lipophilicity", as explained above, Won also teaches the polymeric particles for efficient entrapment of the active ingredient and timed release of the same at a desired release rate. Additionally, Won also suggests employing solvents or vehicle such that the release of active agent does not occur all at once. Won also suggests that the release also depends on the pore volume and pore size. Thus, the prior art of record also suggests controlling the release of the active ingredient as a function of solvent that dissolution of the active (by diffusion) and the pore size and volume of the polymer. On

the other hand, applicants only state that the lipophilicity claimed "may" facilitate particularly ready, uniform and is thermodynamically favorable mixing of the formulations or "may" ensure that a desired rate of release from the polymeric delivery system is consistently achieved after the formulations have been mixed and applied to the skin. Applicants have not shown any unexpected advantage in both the carrier bases having substantially same lipophilicity or with the claimed viscosity ranges. Whereas, Won teaches the same argued advantages i.e., effective timed release of the active agent and reduced irritation of the product (see the explanation in the body of the rejection). A skilled artisan would achieve the same result i.e., a controlled release of the active entrapped in the porous polymers, of different emulsions, by choosing the appropriate solvent or carriers and thus achieve the same end result as that achieved by applicants. Applicants argue that where the carrier is a very good solvent for the active ingredient - the majority - if not all - of the active ingredient will be lost from the delivery system, causing essentially the entire amount of active ingredient to be delivered immediately (see response of 12-18-09, page 10), which is also recognized by Won (col. 8, L 5-13).

Conclusion

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611
April 9, 2010